

SEQUENCE LISTING

<110> KYOWA HAKKO KOGYO CO., LTD

<120> AGENT FOR TREATING ARTHRITIS

<130> 1442

<150> JP2001-400677

<151> 2001-12-28

<160> 51

<170> PatentIn version 3.1

<210> 1

<211> 420

<212> DNA

<213> Mus musculus

<220>

<223> Inventor: Tamura, Tadafumi; Uchii, Masako; Toshio, Suda
Inventor: Ichiro, Miki; Akira, Tanaka

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<221> source

<222> (1)..(420)

<223> /organism="Mus musculus"

<220>

<221> CDS

<222> (1)..(420)

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<222> (1)..(57)

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Met Glu Trp Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly
1 5 10 15

gtc tac tcc cag gtt cag ctg cag cag tct gga gct gag gtg gcg agg 96
Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg
20 25 30

ccc ggg gct tca gtg aaa ctg tcc tgc aag gct tct ggc tac acc ttc 144
Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe
35 40 45

act gac tac tat cta aac tgg gtg aag cag agg tct gga cag ggc ctt 192
Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu
50 55 60

gag tgg att gga gag att gat cct gga agt gat agt ata tat tat aat 240
Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn
65 70 75 80

gaa aac ttg gag ggc agg gcc aca ctg act gca gac aaa tcc tcc agc 288
Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser
85 90 95

aca gcc tac atg cag ctc aac agc ctg aca tct gag gac tct gca gtc 336
Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
100 105 110

tat ttc tgt gca aga tat ggg tat tct aga tac gac gta agg ttt gtc 384
Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val
115 120 125

tac tgg ggc caa ggg act ctg gtc act gtc tct aca 420
Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr

130

135

140

<210> 2

<211> 140

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<213> Mus musculus

<220>

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<222> (1)..(19)

<400> 2

Met Glu Trp Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly

1

5

10

15

Val Tyr Ser Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg

20

25

30

Pro Gly Ala Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe

35

40

45

Thr Asp Tyr Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu

50

55

60

Glu Trp Ile Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn

65

70

75

80

Glu Asn Leu Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser

85

90

95

Thr Ala Tyr Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val
 100 105 110

Tyr Phe Cys Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val
 115 120 125

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Thr
 130 135 140

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<220>
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 Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala
 1 5 10 15

tcc agg agt gat gtt ttg atg acc caa act cca ctc tcc ctg cct gtc	96
Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val	
20 25 30	
agt ctt gga gat caa gcc tcc atc tct tgc aga tct agt cag agt ctt	144
Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu	
35 40 45	
gta cat agt aat gga aga acc tat tta gaa tgg tac ctg cag aaa cct	192
Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro	
50 55 60	
ggc cag tca cca aag gtc ctg atc tac aaa gtt tcc aac cga att tct	240
Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser	
65 70 75 80	
ggg gtc cca gac agg ttc agt ggc agt gga tca ggg aca gat ttc aca	288
Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr	
85 90 95	
ctc aaa atc agc aga gtg gag gct gag gat ctg gga gtt tat ttc tgc	336
Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys	
100 105 110	
ttt cag ggt tca cat gtt ccg tac acg ttc gga ggg ggg acc aag ctg	384
Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu	
115 120 125	
gaa ata aaa	393
Glu Ile Lys	
130	

<210> 4

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<213> Mus musculus

<220>

<221> SIGNAL

<222> (1)..(19)

<400> 4

Met Lys Leu Pro Val Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala

1

5

10

15

Ser Arg Ser Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val

20

25

30

Ser Leu Gly Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu

35

40

45

Val His Ser Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro

50

55

60

Gly Gln Ser Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser

65

70

75

80

Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr

85

90

95

Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys

100

105

110

Phe Gln Gly Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu

115

120

125

Glu Ile Lys

130

<210> 5

<211> 121

<212> PRT

<213> Mus musculus

<400> 5

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala

1

5

10

15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr

20

25

30

Tyr Leu Asn Trp Val Lys Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile

35

40

45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu

50

55

60

Glu Gly Arg Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr

65

70

75

80

Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys

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95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly

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105

110

Gln Gly Thr Leu Val Thr Val Ser Thr

115

120

<210> 6
<211> 112
<212> PRT
<213> Mus musculus

<400> 6

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 7

<211> 5
<212> PRT
<213> Mus musculus

<400> 7
Asp Tyr Tyr Leu Asn
1 5

<210> 8
<211> 17
<212> PRT
<213> Mus musculus

<400> 8
Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu Glu
1 5 10 15

Gly

<210> 9
<211> 12
<212> PRT
<213> Mus musculus

<400> 9
Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr
1 5 10

<210> 10
<211> 16
<212> PRT
<213> Mus musculus

<400> 10

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Arg Thr Tyr Leu Glu

1

5

10

15

<210> 11

<211> 7

<212> PRT

<213> Mus musculus

<400> 11

Lys Val Ser Asn Arg Ile Ser

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<210> 12

<211> 9

<212> PRT

<213> Mus musculus

<400> 12

Phe Gln Gly Ser His Val Pro Tyr Thr

1

5

<210> 13

<211> 22

<212> DNA

<213> Artificial

<220>

<223> a primer for amplification of KM1334 VH

<400> 13

ctgaattcgc ggccgctagt cc

<210> 14

<211> 39

<212> DNA

<213> Artificial

<220>

<223> a primer for amplification of KM1334 VH

<400> 14

atgggccctt ggtggaggct gtagagacag tgaccagag

39

<210> 15

<211> 22

<212> DNA

<213> Artificial

<220>

<223> a primer for amplification of KM1334 VL

<400> 15

ctgaattcgc ggccgctgct gt

22

<210> 16

<211> 28

<212> DNA

<213> Artificial

<220>

<223> a primer for amplification of KM1334 VL

<400> 16

atcgtacgtt ttatttccag ctgtgtcc

28

<210> 17

<211> 25

<212> PRT

<213> Artificial

<220>

<223> human FGF-8 peptide (amino acids residues 23-46) added an
cysteine residue at its C-terminus

<400> 17

Gln Val Thr Val Gln Ser Ser Pro Asn Phe Thr Gln His Val Arg Glu
1 5 10 15

Gln Ser Leu Val Thr Asp Gln Leu Cys
20 25

<210> 18

<211> 121

<212> PRT

<213> Artificial

<220>

<223> HV.0, a designed amino acid sequence of VH of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 18

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 19

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.0, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 19

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly

1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 20

<211> 121

<212> PRT

<213> Artificial

<220>

<223> HV.6, a designed amino acid sequence of VH of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 20

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala

1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr

20 25 30

Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile

35 40 45

Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu

50 55 60

Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr

65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys

85 90 95

Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly

100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser

115 120

<210> 21

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.6, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 21

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 22

<211> 504

<212> DNA

<213> Artificial

<220>

<223> a DNA encoding HV.0

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<221> CDS

<222> (47)..(466)

<220>

<221> sig_peptide

<222> (47)..(103)

<400> 22

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Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc 103
Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser
-15 -10 -5 -1

cag gtg cag ctg gtg cag tct ggg gct gag gtg aag aag ccc ggg gcc 151
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac 199
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

tat cta aac tgg gtg cgg cag gcc ccc gga caa ggg ctt gag tgg atg 247
Tyr Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg 295
 Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu
 50 55 60

gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac 343
 Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr
 65 70 75 80

atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat tac tgt 391
 Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc 439
 Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly
 100 105 110

cag gga acc ctg gtc acc gtc tcc tca gcctccacca agggcccact 486
 Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

agtcgtgact gggaatac 504

<210> 23

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 23

caggaaacag ctatgacgaa ttgcggcgc cacactgact ctaaccatgg aatggatctg 60

gatctttctc ttcttctct caggaaactac aggtgtctac tcccagggtgc agctgggtgca 120

gtctggggct gaggtgaaga a 141

<210> 24

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 24

aggatgatc tctcccatcc actcaagccc ttgtccgggg gcctgccgca cccagtttag 60

atagtagtca gtgaagggtg atccagaagc cttgcaggag accttcactg aggccccggg 120

cttcttcacc tcagccccag a 141

<210> 25

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.0

<400> 25

ggatgggaga gatcgatcct ggaagtgata gtatatatta taatgaaaac ttggagggca 60

gagtcacgat taccgcggac acatccacga gcacagccta catggagctg agcagcctga 120

gatctgagga cacggccgtg t 141

<210> 26

<211> 141

<212> DNA

<213> Artificial

<220>

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<400> 26

gttttcccag tcacgactag tgggcccttg gtggaggctg aggagacggt gaccagggtt 60

ccctggcccc agtagacaaa ccttacgtcg tatctagaat acccatactc cgcacagtaa 120

tacacggccg tgcctcaga t 141

<210> 27

<211> 504

<212> DNA

<213> Artificial

<220>

<223> a DNA encoding HV.6

<220>

<221> CDS

<222> (47)..(466)

<220>

<221> sig_peptide

<222> (47)..(103)

<400> 27

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Met Glu Trp

atc tgg atc ttt ctc ttc ttc ctc tca gga act aca ggt gtc tac tcc	103
Ile Trp Ile Phe Leu Phe Phe Leu Ser Gly Thr Thr Gly Val Tyr Ser	
-15 -10 -5 -1	
cag gtg cag ctg gtg cag tct ggg gct gag gtg gcg agg ccc ggg gcc	151
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Ala Arg Pro Gly Ala	
1 5 10 15	
tca gtg aag gtc tcc tgc aag gct tct gga tac acc ttc act gac tac	199
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr	
20 25 30	
tat cta aac tgg gtg cgg cag agg tct gga caa ggg ctt gag tgg att	247
Tyr Leu Asn Trp Val Arg Gln Arg Ser Gly Gln Gly Leu Glu Trp Ile	
35 40 45	
gga gag atc gat cct gga agt gat agt ata tat tat aat gaa aac ttg	295
Gly Glu Ile Asp Pro Gly Ser Asp Ser Ile Tyr Tyr Asn Glu Asn Leu	
50 55 60	
gag ggc aga gtc acg att acc gcg gac aca tcc acg agc aca gcc tac	343
Glu Gly Arg Val Thr Ile Thr Ala Asp Thr Ser Thr Ser Thr Ala Tyr	
65 70 75 80	
atg gag ctg agc agc ctg aga tct gag gac acg gcc gtg tat ttc tgt	391
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Phe Cys	
85 90 95	
gcg aga tat ggg tat tct aga tac gac gta agg ttt gtc tac tgg ggc	439
Ala Arg Tyr Gly Tyr Ser Arg Tyr Asp Val Arg Phe Val Tyr Trp Gly	
100 105 110	
cag gga acc ctg gtc acc gtc tcc tca gcctccacca aggcccact	486
Gln Gly Thr Leu Val Thr Val Ser Ser	
115 120	

agtcgtgact gggaaaac

504

<210> 28

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 28

caggaaacag ctatgacgaa ttgcggccg cacactgact ctaaccatgg aatggatctg 60

gatctttctc ttcttcctct caggaactac aggtgtctac tcccagggtc agctggtgca 120

gtctggggct gaggtggcga g 141

<210> 29

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 29

aggatcgatc tctccaatcc actcaagccc ttgtccagac ctctgccgca cccagtttag 60

atagtagtca gtgaagggtg atccagaagc cttgcaggag accttcactg aggccccggg 120

cctcgccacc tcagccccag a 141

<210> 30

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 30

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gatctgagga cacggccgtg t 141

<210> 31

<211> 141

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding HV.6

<400> 31

gttttcccag tcacgactag tgggcccttg gtggaggctg aggagacggt gaccagggtt 60

ccctggcccc agtagacaaa cttacgtcg tatctagaat acccatatct cgcacagaaa 120

tacacggccg tgcctcaga t 141

<210> 32

<211> 459

<212> DNA

<213> Artificial

<220>

<223> a DNA encoding LV.0

<220>

<221> CDS

<222> (40)..(432)

<220>

<221> sig_peptide

<222> (40)..(96)

<400> 32

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caggaaacag ctatgacgaa ttcaggttgc ctcctcaaa atg aag ttg cct gtt      54
                                   Met Lys Leu Pro Val
                                   -15
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agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat atc      102
Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Ile
      -10              -5              -1  1
```

```
gtg atg act cag tct cca ctc tcc ctg ccc gtc acc cct gga gag ccg      150
Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro
      5              10              15
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```
gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga      198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly
      20              25              30
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```
aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca cag      246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
      35              40              45              50
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ctc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg      294
Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg
      55              60              65
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ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg	342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg	
70 75 80	

gtg gag gct gag gac gtc ggg gtt tat tac tgc ttt cag ggt tca cat	390
Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly Ser His	
85 90 95	

gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa	432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
100 105 110	

cgtacgacta gtcgtgactg ggaaaac	459
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<210> 33
 <211> 130
 <212> DNA
 <213> Artificial

<220>
 <223> a synthetic DNA for construction of a DNA encoding LV.0

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ttggtgctga tgttctggat tctgcttcc aggagtata tcgtgatgac tcagtctcca	120
ctctccctgc	130

<210> 34
 <211> 130
 <212> DNA
 <213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 34

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actctgacta gatctgcagg agatggaggc cggctctcca ggggtgacgg gcaggagag 120

tggagactga 130

<210> 35

<211> 130

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 35

tgcagaagcc aggccagtct ccacagctcc tgatctataa agtttccaac cgaatttctg 60

gggtcccaga caggttcagt ggcagtggat ccgggacaga ttccacactg aaaatcagca 120

gggtggaggc 130

<210> 36

<211> 129

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.0

<400> 36

gttttcccag tcacgactag tcgtacgttt gatttccacc ttggtccctt ggccgaacgt 60

gtacggaaca tgtgaaccct gaaagcagta ataaaccccg acgtcctcag cctccaccct 120

gctgatttt 129

<210> 37

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<220>

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<222> (40)..(432)

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<222> (40)..(96)

<400> 37

caggaaacag ctatgacgaa ttcaggttgc ctcctcaaa atg aag ttg cct gtt 54

Met Lys Leu Pro Val

-15

agg ctg ttg gtg ctg atg ttc tgg att cct gct tcc agg agt gat gtt 102

Arg Leu Leu Val Leu Met Phe Trp Ile Pro Ala Ser Arg Ser Asp Val

-10

-5

-1 1

gtg atg act cag tct cca ctc tcc ctg ccc gtc agt ctt gga gag ccg 150

Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly Glu Pro

5

10

15

gcc tcc atc tcc tgc aga tct agt cag agt ctt gta cat agt aat gga	198
Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly	
20 25 30	
aga acc tat tta gaa tgg tac ctg cag aag cca ggc cag tct cca aag	246
Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Lys	
35 40 45 50	
gtc ctg atc tat aaa gtt tcc aac cga att tct ggg gtc cca gac agg	294
Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro Asp Arg	
55 60 65	
ttc agt ggc agt gga tcc ggg aca gat ttc aca ctg aaa atc agc agg	342
Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg	
70 75 80	
gtg gag gct gag gac gtc ggg gtt tat ttc tgc ttt cag ggt tca cat	390
Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly Ser His	
85 90 95	
gtt ccg tac acg ttc ggc caa ggg acc aag gtg gaa atc aaa	432
Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys	
120 125 130	
cgtacgacta gtcgtgactg ggaaaac	459

<210> 38

<211> 130

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 38

caggaaacag ctatgacgaa ttcaggttgc ctctcaaaa tgaagttgcc tgtaggctg 60

ttggtgctga tgttctggat tctgcttcc aggagtgatg ttgtgatgac tcagtctcca 120

ctctccctgc 130

<210> 39

<211> 130

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 39

agactggcct ggcttctgca ggtaccattc taaatagggt cttccattac tatgtacaag 60

actctgacta gatctgcagg agatggaggc cggctctcca agactgacgg gcagggagag 120

tggagactga 130

<210> 40

<211> 130

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 40

tgcagaagcc aggccagtct ccaaagggtcc tgatctataa agtttccaac cgaatttctg 60

gggtcccaga caggttcagt ggcagtggat ccgggacaga tttcacactg aaaatcagca 120

gggtggaggc 130

<210> 41

<211> 129

<212> DNA

<213> Artificial

<220>

<223> a synthetic DNA for construction of a DNA encoding LV.6

<400> 41

gttttcccag tcacgactag tcgtacgttt gatttccacc ttggtcctt ggccgaacgt 60

gtacggaaca tgtgaaccct gaaagcagaa ataaaccccg acgtcctcag cctccaccct 120

gctgatttt 129

<210> 42

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.4-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 42

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly

1

5

10

15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 43

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> LV.4-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 43

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 44

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.3-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 44

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 45

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.3-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 45

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly

1

5

10

15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser

20

25

30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser

35

40

45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro

50

55

60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile

65

70

75

80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly

85

90

95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys

100

105

110

<210> 46

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.2-1, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 46

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 47

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.2-2, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 47

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 48

<211> 39

<212> DNA

<213> Artificial

<220>

<223> a primer for construction of DNA encoding LV.3-1

<400> 48

atggtacctg cagaagccag gccagtctcc acaggtcct

39

<210> 49

<211> 39

<212> DNA

<213> Artificial

<220>

<223> a primer for construction of DNA encoding LV.2-2

<400> 49

atggtacctg cagaagccag gccagtctcc acaggtcct

39

<210> 50

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.4-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 50

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly

1

5

10

15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Phe Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 51

<211> 112

<212> PRT

<213> Artificial

<220>

<223> LV.3-3, a designed amino acid sequence of VL of
an anti-FGF-8 CDR-grafted neutralizing antibody

<400> 51

Asp Ile Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Asn Gly Arg Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Val Leu Ile Tyr Lys Val Ser Asn Arg Ile Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110